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Com-1 in breast cancer

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Valerie Speirs,[Aff1]

[Aff1] Molecular Medicine Unit, University of Leeds, UK

Keywords

com1, metastasis, uPA

Introduction

The process of metastasis requires multiple sequential steps. Factors involved in this process include components of the well-characterised urokinase pathway, eg urokinase-type plasminogen activator (uPA), which converts plasminogen into plasmin. uPA activity is controlled by plasminogen activator inhibitor 1 (PAI-1) and its cell surface receptor, uPAR. High expression levels of these factors are associated with reduced survival of breast cancer patients. Recently a novel gene, *com1*, was identified. The *com1* gene is upregulated in breast cancer cells upon formation of experimental metastases and is presumed to mediate the growth response of breast cancer cells. Interaction of *com1*product with members of the urokinase pathway may contribute to enhanced tumour aggressiveness.

Aims

To explore the biological role of *com1*.

Comments

Tumour growth and metastasis are controlled by a number of proteolytic enzymes and growth factors. This paper explores further the biological role of a recently described "candidate of metastasis" gene, com1. Originally believed to distinguish breast cells with metastatic potential from those without (see Additional information), it now appears com1 may mediate some of the earlier events associated with metastasis. Understanding how com1 is regulated will be an important step in defining early and late events in the metastatic process.

Methods

Total RNA was extracted from 81 breast tumours and 27 samples of uninvolved adjacent normal breast tissue. mRNA transcripts of com1, uPAR, uPA and PAI-1 genes were determined by northern blotting. Expression levels were compared with conventional prognostic variables to determine correlations.

Results

Levels of com1 mRNA were significantly higher in tumours than in adjacent normal tissues. Similar expression patterns were observed for uPAR and uPA, but no differences were found in expression of PAI-1 between tumour and normal tissue. No correlation was observed between expression of *com1* and mRNA levels of uPA, uPAR or PAI-1. Similarly, no correlations were found between tumour *com1* expression and histological and biochemical prognostic variables. Comparing the impact of expression of these genes on survival, high uPAR mRNA expression was associated with shorter overall survival; a similar but nonsignificant trend was seen with uPA. mRNA expression of *com1*or PAI-1 genes had no effect on patient survival.

Discussion

The *com1* gene is overexpressed in primary breast tumours, perhaps due to increased tumour growth following malignant transformation. The lack of any significant correlation between *com1* and prognostic outcome suggests a function of *com1*in the early development of breast tumours.

Additional information

Ree AH *et al*, Expression of a novel factor in human breast cancer cells with metastatic potential. *Cancer Res* 1999, **59**:4675-4680 (PubMed abstract)

References

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